

APPENDIX A: INCLUDED ARTICLES

1. Abatemarco D, Perera S, Bao SH, et al. Training Augmented Intelligent Capabilities for Pharmacovigilance: Applying Deep-learning Approaches to Individual Case Safety Report Processing. *Pharmaceut Med.* 2018;32(6):391-401. doi:10.1007/s40290-018-0251-9
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APPENDIX B: DATA COLLECTION VARIABLES

#	Variable Name	Examples of values	Type/Description
1	Deep learning algorithm(s)	LSTM, GRU, CNN	List
2	DL package(s)	Tensorflow, Keras, Theano	List
3	Embedding techniques	word2vec, GLoVe+position	List
4	Unlabeled training corpus (e.g., for embeddings)	MIMIC, Wikipedia	List
5	Medical knowledge resources	UMLS, Task-specific schema	List
6	Was clinical knowledge integrated in DL?	No, Yes in system, Yes affecting architecture	Multiple choice
7	NLP Task(s)	Text Classification, Entity Normalization	Selection grid
8	NLP packages	cTAKES, NLTK, SpaCy	List
9	Main Clinical Task	Adverse Drug Events, Phenotyping	String
10	Task dataset source	i2b2 challenges, Intra-institutional data	List
11	Task dataset size	10,024 sentences, 1,600 patients	List
12	Task dataset type of text	Radiology reports, Discharge summary	List
13	Task dataset language	English, Thai, Chinese	List
14	Was there multimodal data present?	Yes, No	Boolean
15	Traditional ML methods integrated with DL?	CRF, Logistic Regression	Selection grid
16	Traditional ML methods compared against DL?	SVM, Random Forest	Selection grid
17	Most successful method (vs. Traditional ML)	Proposed DL, Traditional ML, Task-specific	Multiple choice
18	Computational equipment	Local CPU, Cloud GPU	Multiple choice
19	Contributed software	Yes, No	Boolean
20	All contributions in paper	Evaluation; Methods variant of DL architecture	List
21	Primary contribution	Application, Methods, Evaluation, Resources	Multiple choice
22	Year	2015, 2016, 2017, 2018, 2019	Number
23	Venue	Journal, Conference	Multiple choice
24	Pre-print status	Yes, No	Boolean
25	Write a sentence appropriate for a Related Work	"This paper builds word representations..."	String

APPENDIX C: ADDITIONAL RESULTS

Deep Learning Techniques

Table 1: Hierarchical normalization of deep learning techniques. The numbers add to more than 212 because multiple techniques may be used in one paper.

Architecture	Method	Freq.
RNN	LSTM	109
	GRU	16
	Vanilla RNN	5
	Tree-LSTM	1
	CNN-LSTM	3
CNN	CNN	80
	CNN-LSTM	3
FFNN	NN	22
Embeddings Only	Embeddings	21
Other	Autoencoder	3
	DBN	3
	Other DL	3
	Capsule	1
	Memory Network	1
	RecursiveNN	1
	Transformer	1

Embeddings



Figure 1: Hierarchical categorization and proportions of unlabeled data resources (excluding articles which did not report the use of large unlabeled corpora).

Medical Knowledge

Table 2: Medical Knowledge Resources used in DL for Clinical NLP papers

Total Papers with Knowledge	38
Custom Lexicon	7
Existing (Non-Standard Lexicon)	3
UMLS	15
ICD-10	6
ICD-9	4
SNOMED-CT	3
RadLex	3
CLEVER	2
ICD-8	1
BI-RADS	1
DSM	1
ICPC-1	1
MedDRA	1
NCI	1
Wikipedia	1

Table 2 shows the numbers of papers that employed medical knowledge, as well as a breakdown by knowledge source. A total of 38 papers used some form of external medical knowledge (i.e., not entirely derived from the training samples). Most of these used only a single source of knowledge, but 6 papers incorporated two separate knowledge sources and 3 papers incorporated three sources. The most frequent knowledge source (n=15) was the Unified Medical Language System (UMLS), though many of the other knowledge sources are components of UMLS, such as ICD (n=11), SNOMED-CT (n=3), MedDRA (n=1), DSM (n=1), and the NCI Thesaurus (n=1). The choice to use a more specific terminology than all of UMLS was typically motivated by the domain of interest (e.g., a psychiatry NLP paper used DSM, the Diagnostic and Statistical Manual of Mental Disorders). Beyond this, radiology terminologies were the most utilized (4 papers). 10 papers used non-standard lexicons for knowledge, either customized for that paper (n=7) or derived from previous papers (n=3).

Implementation

Table 3: The top ranked deep learning libraries and NLP tools for deep learning in clinical NLP.

	Deep learning libraries (#, % of 212)	NLP tools (#, % of 212)
1	Tensorflow ¹ (46, 21.7%)	Gensim ² (15, 7.1%)
2	Keras ³ (32, 15.1%)	cTAKES ⁴ (10, 4.7%)
3	Theano ⁵ (14, 6.6%)	NLTK ⁶ (10, 4.7%)
4	Torch ⁷ (6, 2.8%)	MetaMap ⁸ (8, 3.8%)
5	Deeplearning4j ⁹ (3, 1.4%)	Stanford CoreNLP ¹⁰ (7, 3.3%)
6	Lasagne ¹¹ (2, 0.9%)	Jieba ¹² (6, 2.8%)

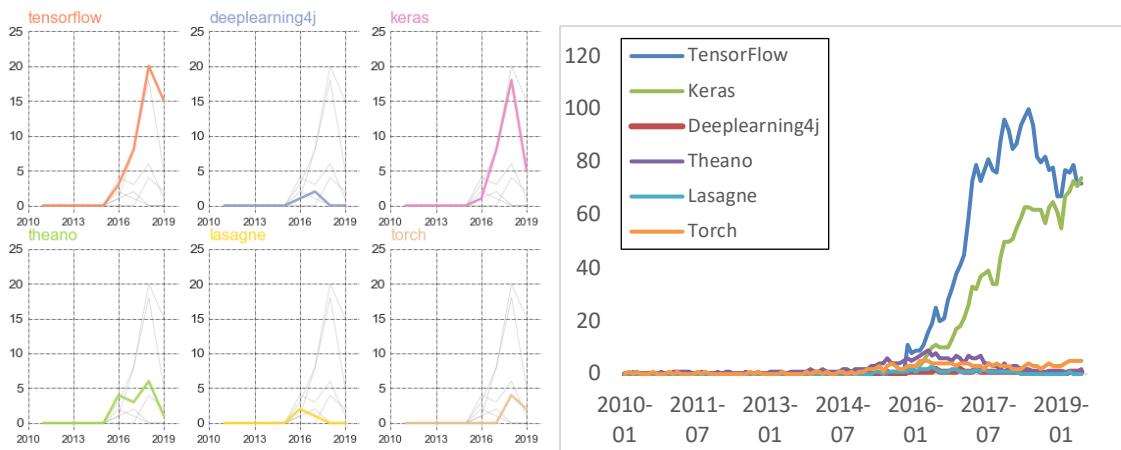


Figure 2: (a) The trends of usage for six most popular deep learning libraries starting from 2010. (b) The trends of searches for these six libraries extracted from Google Trends.

From Table 3 and Figure 2a, the popular deep learning libraries Tensorflow and Keras boast increasing trends starting from the year 2015. As Tensorflow is attracting more and more attention in both industry and the academic, it is also widely applied in the clinical NLP domain. Keras is a powerful and easy-to-use library and it has the backend of both Tensorflow and Theano. It is also one of the primary selections for multidisciplinary research. Theano ranks third in the overall user quantity but it looks like the usage of it was not stable over the years and it goes in a decreasing trend. Lasagne is built on top of Theano and can be considered as a member of the Theano family. Our statistics (Figure 2a) are consistent with the searching trends to a great extent under the category of Machine Learning and Artificial Intelligence from Google Trends (Figure 2b). However, there is still a large proportion of papers (47.6%) which did not clearly report the deep learning libraries they used.

¹ <https://www.tensorflow.org/>

² <https://radimrehurek.com/gensim/>

³ <https://keras.io/>

⁴ <https://ctakes.apache.org/>

⁵ <http://deeplearning.net/software/theano/>

⁶ <https://www.nltk.org/>

⁷ <http://torch.ch/>

⁸ <https://metamap.nlm.nih.gov/>

⁹ <https://deeplearning4j.org/>

¹⁰ <https://stanfordnlp.github.io/CoreNLP/>

¹¹ <https://lasagne.readthedocs.io/en/latest/>

¹² <https://github.com/fxsjy/jieba>

Task Dataset Language over Time

Below, we have calculated from the raw data how the language-related publications have progressed over time.

Table 4: The number of studies with task datasets in each natural language, split by year of publication. This is raw data, unnormalized for multiple languages in one paper.

<i>Task dataset language</i>	2003	2011	2014	2015	2016	2017	2018	2019	Total
Chinese			1	1	3	5	17	14	41
Dutch								1	1
English	1	1	1	2	16	36	68	22	147
English, Chinese					1				1
English, French						2			2
English, Thai							1		1
Finnish				2		1	1		4
German							1		1
Italian						1	1		2
Japanese					2		2		4
Not clearly reported						1	1		2
Spanish							4		4
Swedish; Spanish								1	1
Grand Total	1	1	2	5	20	46	98	38	211

This shows that few French articles were included in this study (because they do not have a deep learning component), though French articles are quite prevalent in broader Clinical NLP. It also shows that even as far back as 2016, there were more Chinese than French articles. This highlights a previously unreported fact about non-English clinical NLP: when dealing with deep learning, Chinese has more representation than French.

Data Size

Table 5: Sizes of labeled datasets, grouped by units given in the literature.

Unit	Min of Size	Median of Size	Max of Size	Count of Size
documents	30	1622.5	100000000	158
sentences	441	10024	5500000	19
patients	21	1600	365446	19
entities	1596	9691.5	95725	6
tokens	10000	108907	613593	5
encounters	42276	62930	314000	4
Other	218	-	4800000	10

Studies reported their dataset sizes in ways that were difficult to normalize. However, many did so in terms of documents (n=158) while some also used sentences (n=19) and patients (n=19) as their dataset units. The broader unit of documents include notes, reports, records, summaries, cases, narratives, texts, charts, certificates, and snippets. The median size of the datasets used by these studies is 1622.5 documents, 10,024 sentences, or 1,600 patients.

Data Subdomain & Modalities

Data came from a wide variety of clinical contexts. The generic designator “Clinical notes” (n=53) is the most used dataset type, followed by other more-general types: discharge summaries (n=38), medical records (n=17), and EHR notes (n=17). Clinical specialties are also well-represented, but with fewer publications, ranging from radiology (n=14) and pathology reports (n=13) to nursing notes (n=7) and psychiatric notes (n=6). Other test- or procedure-specific note types were present as well: CT reports (n=4), breast imaging or MIR or ECG (for each, n=3), or patient safety report or ECHO or ultrasound report or mammography report (for each, n=2).

While the majority of the studies stick with using only the free-text data (n=203), a few utilized structured data beyond demographics or timestamps (n=4), and images (n=2).

Contributions

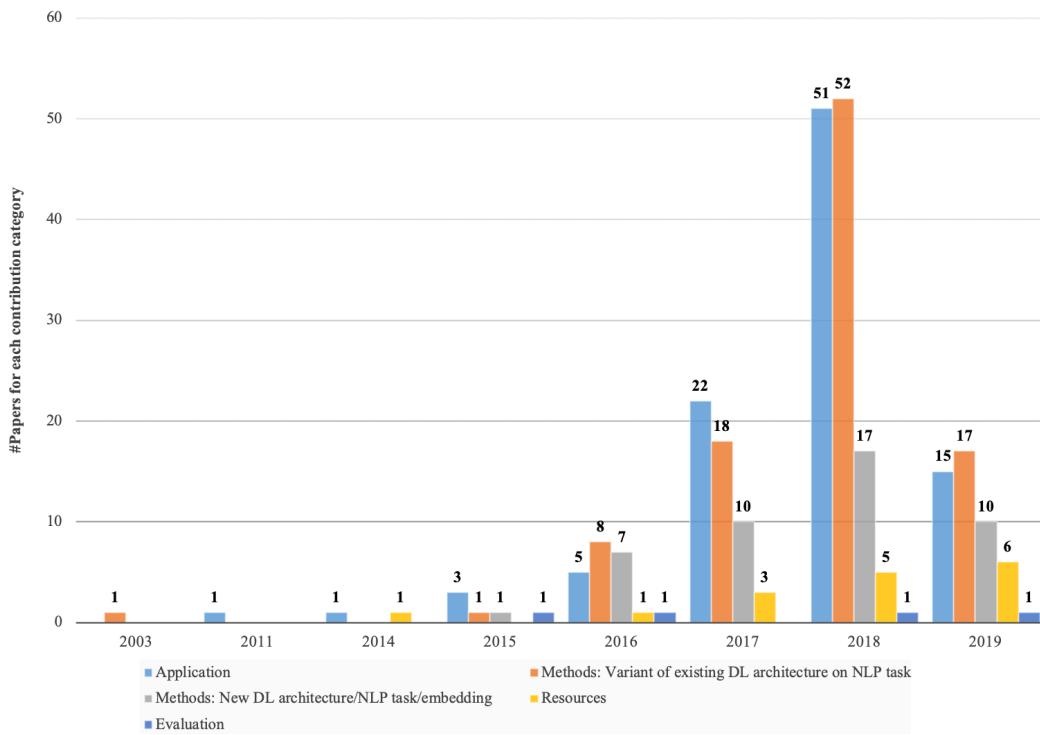


Figure 3: Distribution of papers per contribution category across time

Figure 3 shows the pattern of the coarse-grained contribution types over time. New Methods in this chart grew more slowly in 2018 than many Methods variants or applications, perhaps pointing to an eventual plateau in innovation (though this is unlikely in 2019, given that the eligibility period ends partway through the year on April 10, 2019).

The main contributions of eligible papers were originally collected as a more fine-grained variable. In terms of these fine-grained main contributions, we observe that majority of the papers used some variant of existing DL architectures ($n=97$), followed by papers where the main focus was on evaluating the DL models on a new labeled dataset ($n=77$). A total of 38 papers implemented new DL architectures, while 21 papers applied DL to either a new domain, language, or clinical setting. Interestingly, we see that only a few papers proposed new embedding techniques ($n=2$) and novel NLP task approaches ($n=5$). Overall, 16 papers contributed new resources, either new dataset ($n=5$), package ($n=6$), or other resources such as lexicon ($n=5$). A total of 4 papers highlighted evaluation methods, 3 from the Informatics community and 1 from the NLP community.

1,2,11,101–110,12,111–120,13,121–130,14,131–140,15,141–150,16,151–160,17,161–170,18,171–180,19,181–190,20,191–200,3,21,201–
210,22,211,212,23–30,4,31–40,5,41–50,6,51–60,7,61–70,8,71–80,9,81–90,10,91–100